REMARKS

Claims 72, and 74 - 91 are pending in the current application. Claim 73 was cancelled. Claims 72, 74, 75, 76, 79, 83, 84 and 90 were amended herein for clarification, and claim 91 was also added for clarification. Support for the amendments and for the additional claim is provided generally in the application and specifically in paragraphs [0028], [0029], [0037], [0058], and [0059]. No new matter has been entered.

Information Disclosure Statement

The Examiner noted at page 2 of the Action that the Information Disclosure Statement provided by applicants on September 10, 2008 "fails to comply" with the requirement that legible copies of foreign and non-patent references be supplied. The Examiner stated that the IDS "has been placed in the application file, but the information referred to therein has not been considered."

To clarify, it is applicants' understanding that, with respect to the September 10, 2008 IDS, the Examiner did in fact consider all of the U.S. patents listed therein. The copy of the September 10, 2008, IDS attached to the current Action includes the Examiner's initials next to the U.S. patent citations; only the non-patent citation "Dow Corning Acrylic Adhesives for Healthcare (2004)" has been struck through. The IDS further includes the caption "ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /T.A./"

Applicants respectfully request reconsideration. All of the wording contained in Applicants' file copy of the Dow Corning Acrylic Adhesives for Healthcare (2004) document is legible. In the next Action, the Examiner is requested to specify what information in that document is deemed to be illegible so that applicants may supply the Examiner with a substitute copy if needed.

Rejections under 35 U.S.C. §§101 & 112

Claim 90 was rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 90 was also rejected under 35 U.S.C. §101, the Examiner asserting that the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process. In response to these rejections, claim 90 has been amended.

Claim 90 has been amended to clarify the claimed method. As currently amended, claim 90 recites "[a]method of delivering the controlled release composition of claim 72 to a substrate comprising: applying the controlled release composition to a dressing; and applying the dressing to the substrate." As a result, it is believed that amended claim 90 recites positive steps delimiting how the method is actually practiced, and it is believed that the Examiner's rejection under 35 U.S.C. §112, second paragraph, is overcome. Similarly, it is believed that amended claim 90 does not recite an improper definition of a process, and thus, the Examiner's rejection of claim 90 under 35 U.S.C. §101 is also believed to be overcome. It is therefore respectfully requested that these rejections be withdrawn.

Rejections under 35 U.S.C.§112

Claim 79 was rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In response to this rejection, claim 79 has been amended and claim 91 has been added.

The Examiner rejected claim 79 under 35 U.S.C. §112, second paragraph, stating that where the applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition. Specifically, the Examiner stated that the accepted meaning of the term "enzyme," recited in claim 79, is "any of numerous complex proteins that are produced by living cells and catalyze specific biochemical reactions at body temperatures." The Examiner argued that because the specification does not clearly redefine the term "enzyme," the recitation of the term in claim 79 followed by a list of non-enzyme proteins rendered the claim unclear as to what applicants regard as enzymes. Specifically, the Examiner stated that claim 79 recites non-enzyme proteins such as "antibodies, polypeptides, peptides, hormones, cytokines, growth factors, biological modulators, and combinations thereof."

Thus, claim 79 has been amended to better comport with the accepted meaning of "enzyme." Specifically, claim 79 has been amended to recite "[a] controlled-release composition as set forth in claim 77 wherein said enzyme is selected from the group of oxidoreductases, transferases, isomerases, ligases, hydrolases, cutinases, oxidases, reductases, hemicellulases, esterases, pectinases, lactases, peroxidases, laccases, catalases, and combinations thereof." As a

result, claim 79 is believed to be in full compliance with 35 U.S.C. §112, second paragraph, and it is respectfully requested that this rejection be withdrawn.

Additionally, claim 91 has been added to further clarify the nature of the "active agent comprising a protein incorporated into said emulsion" as recited in claim 72. Claim 91 recites "[t]he controlled-release composition as set forth in claim 72 wherein said protein is selected from the group of antibodies, polypeptides, peptides, hormones, cytokines, growth factors, biological modulators, and combinations thereof." Support for this claim may be found in the specification in [0058]. No new matter has been entered. Accordingly, allowance of this claim is respectfully solicited.

Rejections under 35 U.S.C. §102

Claims 72-79, 81, 83-84, and 87-88 were rejected under 35 U.S.C. §102(b) as being anticipated by Foldvari et al. (US 5993852). In response to this rejection, claims 72, 74-76, and 83-84 have been amended and claim 73 has been cancelled.

The Examiner argued that Foldvari discloses a composition that includes an oil-in-water (O/W) emulsion for transdermal administration and also teaches a transdermal device for administration of the composition. With specific regard to claim 72, the Examiner stated that Foldvari teaches a composition comprised of an oil-in-water emulsion that additionally includes an immunogen (i.e. protein) incorporated into the emulsion. The Examiner further stated that Foldvari discloses a hydrophilic solvent (i.e. being substantially free of lipophilic solvent).

The Examiner also stated that the membrane and reservoir disclosed in Foldvari form the controlled release layer of the composition and that the composition is administered transdermally (i.e. topically to the skin). The Examiner argued that although Foldvari does not disclose the emulsion as being formed by mechanical inversion, the process by which the composition is made is irrelevant where the composition disclosed by the prior art is structurally equivalent to the composition that the applicant is claiming.

In response, claim 72 has been amended to recite "[a] controlled-release composition for topical application to a substrate, said composition comprising: an oil-in-water emulsion substantially free of lipophilic solvent and formed by mechanical inversion of a water-in-oil emulsion and an active agent comprising a protein incorporated into said emulsion, wherein said emulsion has a hydrophilic phase comprising said active agent, water, and a carrier, and a

hydrophobic phase comprising a silicone component." Foldvari does not teach or suggest "a hydrophobic phase comprising a silicone component" as recited in amended independent claim 72. As a result, the claim is believed to be patentable over Foldvari.

The Examiner also rejected dependent claims 73 and 83-84 as being anticipated by Foldvari. Specifically, the Examiner stated that Foldvari teaches the active agent (i.e. immunogen) as being able to be entrapped in the water phase (hydrophilic phase) of the oil-in-water emulsion depending on the physiochemical properties of the immunogen. Furthermore, the Examiner argued that Foldvari discloses the hydrophilic phase as being prepared in Example 1 by mixing components including propylene glycol (carrier) and water. The Examiner also asserted that the silicone component, more specifically polydimethylsiloxane, is in the form of a pressure sensitive adhesive. In response to this rejection, claim 72 has been amended and claim 73 has been cancelled. Although the Examiner's rejection of claim 73 as being anticipated by Foldvari is believed to have been disposed by the cancellation of claim 73, the language of claim 73 has been incorporated into amended claim 72. Thus, the following remarks are intended to address the Examiner's rejection of claim 73, elements of which are now recited in amended claim 72.

The Examiner's reasoning is flawed in asserting that Foldvari discloses the silicone component recited in amended claim 72. While the Examiner is correct in her assertion that Foldvari discloses a silicone component in the form of a pressure sensitive adhesive, Foldvari fails to disclose "[a] controlled release composition . . . [comprising] an oil-in-water emulsion . . . wherein said emulsion has a hydrophilic phase comprising said active agent, water, and a carrier, and a hydrophobic phase comprising a silicone component." More specifically, Foldvari fails to disclose "a hydrophobic phase comprising a silicone component."

The silicone component disclosed in Foldvari is an adhesive layer 50 made from a pharmaceutically acceptable pressure sensitive adhesive, such as polydimethylsiloxane. (*See* Column 9, lines 49-53). The adhesive layer 50 is a means by which a transdermal device is affixed to the skin. (*See* Column 9, lines 49-50). However, the adhesive layer is not located within the hydrophobic phase of the emulsion as recited in claim 72. Rather, the adhesive layer is separate from the emulsion component of the biphasic lipid vesicles disclosed in Foldvari.

Specifically, the biphasic lipid vesicles disclosed in Foldvari include an oil-in-water emulsion 22, 24, 26 in the central core compartment of the lipid vesicle and in the aqueous space

separating the lipid bilayers 12, 14. (*See* FIG. 1 and Column 5, lines 49-52). The transdermal device 40, which the Examiner asserts comprises the silicone component recited in amended claim 72, includes a reservoir 42 adapted to retain during storage and release in operation lipid vesicles containing an entrapped antigen. (*See* Column 9, lines 9-10 and 15-16). The reservoir 42 is defined by an impermeable backing layer 44 and a membrane 46. (*See* FIG. 3A and Column 9, lines 16-17). The adhesive layer 50, made from a pharmaceutical acceptable pressure sensitive adhesive, is a means for affixing the device to the skin of the subject. (*See* FIG. 3A).

Thus, in Foldvari, the adhesive layer 50 is separated from the reservoir 42 adapted to retain lipid vesicles, where the emulsion is located. Consequently the pressure sensitive adhesive, such as polydimethylsiloxane, is not located within the hydrophobic component of the emulsion, as recited in amended claim 72. Foldvari, therefore, fails to teach or suggest "a hydrophobic phase comprising a silicone component " as recited in amended claim 72.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Thus, as Foldvari fails to disclose "a hydrophobic phase comprising a silicone component," the Examiner's rejection of claim 72 is believed to be overcome. As previously presented, claims 74-76 and 83-84 depend from claim 73. Because claim 73 was cancelled, claims 74-76 and 83-84 have been amended such that they depend from claim 72. Because claims 74-79, 81, 83-84 and 87-88 depend from amended claim 72, it is believed that the Examiner's rejection of these claims is also overcome. Additionally, the cancellation of claim 73 is believed to render the Examiner's rejection of claim 73 moot. Thus, it is respectfully solicited that this rejection be withdrawn.

Rejections under 35 U.S.C. §103

Claim 89 was rejected under 35 U.S.C. §103(a) as being unpatentable over Foldvari and Mackles et al. (US 5178881). Claims 80, 82 and 85-86 were rejected under 35 U.S.C. §103(a) as being unpatentable over Foldvari and Bott et al. (US 2003/0180281) as evidenced by Kanios et al. (US 6337086). These rejections are respectfully traversed.

Claim 89 recites "[a] controlled release composition as set forth in claim 87 wherein said controlled-release layer is dry in said dressing such that said controlled-release layer is free of water after said controlled-release layer is formed by said controlled-release composition." The controlled release layer recited in claim 87 is "formed from said controlled release composition of claim 72." The Examiner rejected claim 89 arguing that Foldvari teaches a composition that includes an oil-in-water (O/W) emulsion for transdermal administration and also teaches a transdermal device for administration of the composition. The Examiner stated that while Foldvari does not teach the controlled release layer (formed from the controlled release composition) as being free of water, Mackles teaches anhydrous topical compositions that dry rapidly on contact. More specifically, the Examiner stated that Mackles teaches anhydrous topical bases that function as delivery systems for medications further in the form of an oil-in-water emulsion. Thus, the Examiner argued that it would have been obvious to a person having ordinary skill in the art to combine the teachings of Foldvari with Mackles because Mackles teaches that the presence of water can result in active ingredient instability.

However, the Examiner's argument that it would have been obvious to combine the teachings of Foldvari with Mackles is flawed for several reasons. Firstly, none of the references, either singularly or in combination, teach or suggest all elements of amended independent claim 72 upon which claim 89 depends. As discussed above, Foldvari fails to disclose "a hydrophobic phase comprising a silicone component" as recited in amended claim 72. Secondly, Mackles, which was narrowly cited for disclosing an anhydrous topical composition, fails to cure the deficiencies of Foldvari. Lastly, the Examiner is incorrect in her assertion that Mackles teaches anhydrous topical bases that function as delivery systems for medications further in the form of an oil-in-water emulsion.

While Mackles does disclose the use of anhydrous compositions suitable for topical application, Mackles does not teach or suggest anhydrous topical bases that function as delivery systems for medications in the form of an oil-in-water emulsion. (*See* Column 1, lines 6-7). Conversely, Mackles distinguishes the disclosed anhydrous composition from efforts to improve dermatological vehicles including oil-in-water emulsion systems in which the oil was dispersed in at least 50% water to form a lotion or a cream. (*See* Column 1, lines 43-47). Additionally, Mackles further distinguishes anhydrous topical bases from the previous systems stating that they suffer from several negatives. (*See* Column 1, lines 53-55). Moreover, Mackles teaches

away from the use of an emulsion disclosing that "emulsions are inherently unstable systems that separate in time." (*See* Column 2, lines 3-4). Thus, contrary to the Examiner's assertions, it would not have been obvious to one of ordinary skill in the art at the time of invention to combine the teachings of Foldvari with the anhydrous feature of the topical composition disclosed in Mackles where Mackles discloses the instability of emulsions.

While Mackles discloses that water sometimes results in active ingredient instability, Mackles teaches away from the use of an emulsion, teaching that emulsions are inherently unstable. Thus, one of ordinary skill in the art would not be led to use an emulsion in a "controlled release layer free of water" as recited in claim 89. Thus, the Examiner's rejection of claim 89 under 35 U.S.C. §103(a) is believed to be overcome.

Lastly, the Examiner rejected claims 80, 82, and 85-86 under 35 U.S.C. §103(a) as being unpatentable over Foldvari and Bott as evidenced by Kanios. Specifically, the Examiner argued that Foldvari teaches a composition that includes an oil-in-water (O/W) emulsion for transdermal administration. The Examiner also conceded that Foldvari does not teach the specific enzymes recited in claim 80, the dispersing agent comprised of a silicone-based surfactant, the pressure sensitive adhesive comprising the reactant product of claim 85, or the silicate resin further defined in claim 86. However, the Examiner suggested that Bott teaches a topical preparation containing a silicone matrix, a hydrophilic carrier, and at least one active agent for release from the preparation which forms an oil-in-water or water-in-oil emulsion.

Claims 80, 82 and 85-86 depend from independent claim 72. Claim 80 recites "[a] controlled-release composition as set forth in claim 77 wherein said enzyme comprises Protease A, Protease B, or LG12." The Examiner stated that Bott teaches proteases such as Protease A or Protease B. However, as previously stated, none of the references, either singularly or in combination, teach or suggest all elements of independent claim 72 as amended from which claim 80 depends. As discussed above, Foldvari fails to disclose "a hydrophobic phase comprising a silicone component" as recited in amended claim 72.

Similarly with regard to claims 82 and 85-86, as previously discussed, Bott was narrowly cited as disclosing a silicone matrix that is selected from high molecular weight polydimethylsiloxanes, loosely or lightly cross-linked silicone elastomers, fillerless elastomers, cellular elastomers, silicone rubbers, silicone pressure sensitive adhesives, and combinations thereof. Claim 82 recites "[a] controlled-release composition as set forth in claim 81 wherein

said dispersing agent comprises a silicone-based surfactant different from said surfactant." Claims 85 recites a "pressure sensitive adhesive compris[ing] the reaction product of; a hydroxy endblocked polydimethylsiloxane polymer, and a hydroxy functional silicate resin." Claim 86 recites a "hydroxy functional silicate resin . . . further defined as a trimethylsiloxy and hydroxy endblocked silicate resin." However, the silicone matrix cited by the Examiner disclosed in Bott is in the external phase of the topical preparation, and, as a result, the hydrophilic carrier containing an active agent is dispersed throughout a silicone matrix. Thus, the silicone matrix cited by the Examiner is not the silicone component recited in claims 85-86 wherein the "emulsion has a hydrophilic phase comprising said active agent, water, and a carrier, and a hydrophobic phase comprising a silicone component."

Therefore, Bott fails to cure the deficiencies of Foldvari in that it does not teach or suggest "a hydrophobic phase comprising a silicone component." As a result, it would not have been obvious to one of ordinary skill in the art at the time the invention was made to devise an emulsion having a hydrophobic phase comprising a silicone component from the biphasic lipid vesicles disclosed in Foldvari and the silicone matrix disclosed in Bott.

The Examiner's citation of Kanios is unclear in that the Examiner did not specifically point out the disclosed elements in Kanios as they relate to the claimed invention. However, if the Examiner cited Kanios for its disclosure of a pressure sensitive adhesive composition with regard to dependent claims 85-86, this narrow citation also fails to cure the deficiencies of Foldvari. Thus, it would not have been obvious to one of ordinary skill in the art to try "[a] controlled-release composition for topical application to a substrate, said composition comprising: an oil-in-water emulsion . . . wherein said emulsion has a hydrophilic phase comprising said active agent comprising a protein, water, and a carrier, and a hydrophobic phase comprising a silicone component" from Foldvari and Bott as evidenced by Kanios. As a result, it is believed that the Examiner's rejection of claims 80, 82, and 85-86 under 35 U.S.C. §103(a) as being unpatentable over Foldvari and Bott as evidenced by Kanios is overcome, and reconsideration of these claims is respectfully solicited.

Conclusion

It is believed that the above represents a complete response to the rejection set forth in the Official Action, and places the present application in condition for allowance. Reconsideration and an early allowance are requested.

Respectfully submitted,
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